Fatty Acids and Cholesterol (2010 Dietary Guidelines Advisory Committee)

Overview, Needs for Future Research

Overview:

The Dietary Guidelines Advisory Committee (DGAC) 2010 first reviewed the 2005 DGAC Report to inform their review process. Several lines of evidence indicate that the type of fat is more important in decreasing metabolic and cardiovascular disease (CVD) risk than the total amount of fat in the diet; therefore, the committee focused their review on the metabolic effect of specific types of fats and fatty acids. Topics in this section on fatty acids and cholesterol that were considered by the 2005 DGAC include:

- Saturated fatty acids (SFA)
- Cholesterol
- Monounsaturated fatty acids (MUFA)
- Omega-6 (n-6) polyunsaturated fatty acids (PUFA)
- Stearic acid
- Trans fatty acids
- Omega-3 (n-3) fatty acids from plants and seafood.

Prior DGAC made recommendations about dietary fat consumption targeting atherosclerotic CVD as the primary disease of concern. The 2010 DGAC continues this focus, but considered additional disease outcomes and intermediate markers of these outcomes. Type 2 diabetes (T2D), as affected by dietary fat, is a new consideration for the 2010 DGAC. Other new questions considered by the 2010 DGAC examined maternal intake of n-3 fatty acids from seafood and the effect on breast milk composition and infant health outcomes; and health effects related to consumption of whole foods high in fat, with the examples being nuts and chocolate *(pending completion of copyediting)*.

For the majority of topics, the conclusions expressed in the 2010 DGAC report are informed by evidence compiled for the 2005 DGAC report, but are based primarily on Nutrition Evidence Library (NEL) evidence gathered and reviewed since 2004. For new or extended topics, the search was extended back further to capture a larger body of evidence, particularly related to diabetic-risk populations. For some topics, a combination of NEL and American Dietetic Association's (ADA) Evidence Analysis Library (EAL) reviews were conducted. For each of the NEL systematic reviews, randomized controlled or clinical trials (RCTs), large non-randomized observational studies, meta-analyses and systematic reviews were included. Health subjects and those with elevated chronic disease risk, including risk of CVD,

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Dietary Guidelines

T2D, and other metabolic risk indicators, were considered for the review.

Needs for Future Research:

1. Determine the benefits and risks of MUFA vs. PUFA as an isocaloric substitute for SFA (see below). Confirm the metabolic pathways through which dietary SFA affect serum lipids, especially as some SFA (e.g., stearic acid) do not appear to affect blood lipid levels.

- **Rationale:** The growing data to support a risk of T2D from SFA consumption indicates the need for fat-modified diets in persons with pre-diabetes, including those with metabolic syndrome, and with established diabetes. Since the ages of onset of T2D now include childhood, studies from adolescence through middle age would be useful to define when SFA-reduced diets would be most effective. Conduct feeding studies using cholesterol from sources other than eggs and funded by non-industry sponsors. Conduct research on low- and high-risk consumers of dietary cholesterol and determine a better definition of hypo- and hyper-responders to dietary cholesterol, with respective underlying genetic polymorphisms. Identify additional subgroups in which dietary cholesterol appears especially harmful with regard to cardiovascular risk
- **Rationale:** Most of the feeding studies with serum lipid and lipoprotein endpoints used eggs as the primary source of cholesterol, and many of the studies were funded by industry. Since the proportion of dietary cholesterol in the US diet supplied by eggs has declined to less than 25%, feeding trials on other dietary sources of cholesterol would be useful. Persons with T2D appear to be a subgroup in which dietary cholesterol is particularly harmful and better understanding of the mechanisms and magnitude of risk is essential, as eggs are an important, low-fat source of protein in T2D patients.

2. Determine the mechanism by which dietary MUFA improve serum lipids, glucose metabolism, insulin levels, homeostatic model assessment (HOMA scores), inflammatory markers and blood pressure in both healthy persons and in persons with T2D. Studies of replacing carbohydrates or other dietary fat with MUFA should include isocaloric substitutions, so as not to be confounded by differences in energy.

- **Rationale**: Understanding the mechanism by which MUFA improve risk of CVD and T2D will enhance our ability to make specific recommendations for MUFA consumption in healthy and at-risk individuals.

3. Determine the mechanism by which dietary PUFA improve serum lipids, glucose metabolism, insulin levels, HOMA scores, inflammatory

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markers, and blood pressure in both healthy persons and in persons with T2D. Studies of replacing carbohydrates or other dietary fat with PUFA should include isocaloric substitutions, so as not to be confounded by differences in energy.

- **Rationale:** Understanding the mechanism by which PUFA improve risk of CVD and T2D will enhance our ability to make specific recommendations for PUFA consumption in healthy and at-risk individuals. PUFA and MUFA have similar benefits as substitutes for SFA and trans fatty acids. Additional isocaloric comparisons of MUFA vs. PUFA on metabolic intermediates and especially on clinical outcomes are needed to differentiate these two classes of fatty acids.

4. Examine stearic acid for its benefits as a solid fat, in contrast to liquid oils high in MUFA and PUFA; include other potential metabolic effects of stearic acid, such as inflammation and coagulation.

- **Rationale**: The benefit of stearic acid is that it has a high melting point and therefore is solid at room temperature, unlike other fatty acids that do not raise blood cholesterol (e.g., MUFA, PUFA). Comparisons of intermediate markers and other effects of stearic acid vs. MUFA and PUFA would clarify ways that it could be best used in a calorie and nutrient-balanced diets.

5. Characterize the difference in metabolic effects and intermediate markers between industrial and ruminant trans fatty acids (rTFA).

- **Rationale**: Since rTFA and industrial trans fatty acids (iTFA) have different chemical structures, better characterization of their metabolic effects though further feeding studies would be warranted.

6. Conduct randomized controlled trials and prospective observational studies in persons with and without CVD on plant compared to marine n-3 fatty acids. Examine diets rich in plant n-3 fatty acids in subjects with and without adequate intake of n-3 fatty acids from marine sources. Examine the mechanism of action of marine vs. plant n-3 fatty acids for
synergies and inhibition.

- **Rationale**: Although there is consistent data on the benefits of n-3 fatty acids from seafood consumption, there is no research on comparing marine vs. plant n-3 fatty acids on intermediate markers and CVD outcomes.

7. Investigate further the opposing interactions of high eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) vs. high methyl mercury, especially in dietary patterns in which these consumptions coexist. Investigate high vs. low DHA-consuming

mothers and infants and the long-term effects on intelligence and other cognitive outcomes.

- **Rationale**: All aspects of the risk to benefit ratio of consumption of EPA + DHA and methyl mercury, both of which can be present in varying amounts in different types of seafood, should be further elucidated. Docosahexaenoic acid appears to be the active nutrient in seafood that provides benefits in infant development. Further studies of the role of DHA in neurodevelopment and dose-response relationships between DHA and health and development outcomes would be useful.

8. Conduct RCTs comparing different types of nuts on intermediate markers, such as serum lipids, and classify each specific type of nut as more or less associated with CVD risk reduction.

- **Rationale**: Additional randomized trials will be required over longer periods of time to determine if nuts confer long-term benefits. It is difficult to distinguish benefits to health and to intermediate metabolites between different types of nuts.

9. Elucidate further the role of polyphenolic compounds as major active ingredients in the health benefits of chocolate. Test different chocolate formulations that are commonly consumed by the general public.

- **Rationale**: Many chocolate and cocoa studies used formulations of chocolate that are not readily available to the consumer and were sponsored by industry. In order to determine the real health benefits of chocolate consumption, chocolate formulations that are available to, and consumed by, the general public need to be tested.